

**REMARKS**

Applicants are amending their claims in order to further clarify the definition of various aspects of the present invention. Specifically, Applicants have amended claim 1 to recite that the microporous compound is H- $\beta$ -form zeolite, and to recite that the H- $\beta$ -zeolite has an Si/Al mole ratio of 10-250; to recite that the oxidizing agent is at least one of iodic acid and periodic acid; and to recite that the reaction step takes place in the presence of acetic acid, in addition to taking place in the presence in acetic anhydride. In light of amendments to claim 1, claims 2, 3, 6 and 12 have been cancelled without prejudice or disclaimer, and claims 4, 7-11 and 18 have been amended to recite H- $\beta$ -form zeolite. In addition, claims 17 and 20 have been cancelled without prejudice or disclaimer, in order to simply issues.

Initially, it is respectfully requested that the present amendments be entered. Noting, for example, previously considered claims 2, 3, 6 and 12, it is respectfully submitted that the present amendments do not raise any new issues, including any issue of new matter; in this regard, and with respect to recitation of H- $\beta$ -form zeolite, note, for example, the Examples in the above-identified application, including, for example, Example 1 on pages 18 and 19 of Applicants' specification. In addition, by further defining materials in the presence of which the reaction step takes place, it is respectfully submitted that the present amendments materially limit any issues remaining in connection with the above-identified application; and, at the very least, present the claims in better form for appeal. Noting the new English translations of applied Japanese Patent Documents, enclosed with the Office Action mailed April 4,

2008, and further contentions by the Examiner in this Office Action mailed April 4, 2008, it is respectfully submitted that the present amendments are timely.

In view of the foregoing, it is respectfully submitted that Applicants have made the necessary showing under 37 C.F.R. §1.116(b)(3); and that, accordingly, entry of the present amendments is clearly proper.

It is respectfully submitted that all of the presently pending claims patentably distinguish over the teachings of the references applied by the Examiner in rejecting claims in the Office Action dated April 4, 2008, that is, the teachings of U.S. Patent No. 5,892,138 to Singh, et al., Japanese Patent Document No. 2003-89673 (Aizawa, et al.), and Japanese Patent Document No. 2003-012597 (Igari, et al.), under the provisions of 35 USC 103.

It is respectfully submitted that the references as applied by the Examiner would have neither taught nor would have suggested such a process for producing 5-iodo-2-methylbenzoic acid as in the present claims, including, inter alia, wherein the reaction step of iodinating 2-methylbenzoic acid is performed in the presence of (1) H- $\beta$ -form zeolite, the H- $\beta$ -form zeolite having an Si/Al mole ratio of 10 to 250, (2) iodine, (3) at least one of iodic acid and periodic acid and (4) both acetic anhydride and acetic acid. See claim 1.

It is emphasized that according to the invention as presently claimed, the reaction step of iodinating 2-methylbenzoic acid is performed in the presence of, inter alia, both acetic anhydride and acetic acid. As seen in the Examples and Comparative Examples of the above-identified application, and as discussed further infra, if materials recited in the present claims (e.g., if the acetic anhydride) are not used, both the yield

and selectivity of 5-iodo-2-methylbenzoic acid and the purity in crystals are reduced together. And if the acetic anhydride and acetic acid are not used, iodine content in the crystals is greatly increased because of a reduction of conversion of iodine. The remaining iodine causes an increase in the load of separation/recovery during the purification step.

Using acetic acid and acetic anhydride together gives not only a very high selectivity, yield and purity, but also very small iodine content in the crystals, which would have neither been disclosed nor suggested by the applied references, discussed infra.

In addition, it is respectfully submitted that these references as applied by the Examiner would have neither taught nor would have suggested such a process for producing 5-iodo-2-methylbenzoic acid as discussed previously, having features as discussed in connection with claim 1, and, additionally, wherein the H- $\beta$ -form zeolite is subjected to calcining after separating and recovering the H- $\beta$ -form zeolite from a reaction mixture resulting from the reaction step. See claim 8, and claims dependent thereon. Calcining of the H- $\beta$ -form zeolite results in prolonging the life of the catalyst, as can be seen in Examples 9-11 on pages 27 and 28 of Applicants' specification, including Tables 3-5, respectively.

Furthermore, it is respectfully submitted that the teachings of the applied references would have neither disclosed nor would have suggested such a process for producing 5-iodo-2-methylbenzoic acid as in the present claims, having features as discussed previously in connection with claim 1, and further including, inter alia (but not limited to), wherein the H- $\beta$ -form zeolite contains an element other than Si, Al, and O,

which form a skeleton thereof, within or outside the skeleton (see claim 4), in particular wherein this element other than Si, Al and O is at least one member selected from among those set forth in claim 5; and/or wherein the H- $\beta$ -form zeolite is separated and recovered from a reaction mixture resulting from the reaction step, followed by re-employment in the reaction step (see claim 7), particularly wherein the separated and recovered H- $\beta$ -form zeolite is washed with acetic acid serving as the solvent (see claim 10); and/or wherein the purification step is crystallization in which a product is precipitated through cooling or addition of water (see claim 13), more particularly, further definition of the purification as in claims 14, 15 and 19.

In addition, and as will be discussed further infra, it is respectfully submitted that the evidence of record, that is, the evidence in the Examples and Comparative Examples in Applicants' specification, establish unexpectedly better results achieved by the present invention, wherein the reaction step of iodinating 2-methylbenzoic acid is performed in the presence of (1) H- $\beta$ -form zeolite, (2) iodine, (3) at least one of iodic acid and periodic acid and (4) both acetic acid and acetic anhydride, as compared with processes of the closest prior art and/or processes even closer than the closest prior art, and based thereon overcomes any possible prima facie case of obviousness established by the teachings of the applied references and clearly supports a conclusion of unobviousness of the present invention. In this regard, it is respectfully submitted that the experimental data in Applicants' specification must be considered in determining obviousness. See In re DeBlauwe, 222 USPQ 191 (CAFC 1984).

The present invention is directed to a process for producing 5-iodo-2-methylbenzoic acid, and to high-purity 5-iodo-2-methylbenzoic acid produced by such process.

As described on pages 1-5 of Applicants' specification, there have been known methods for synthesizing 5-iodo-2-methylbenzoic acid. However, these various known methods have problems. For example, various of the methods have a low yield and/or low selectivity and /or produce a low purity product, e.g., producing relatively large amounts of 3-iodo-2-methylbenzoic acid rather than 5-iodo-2-methylbenzoic acid. In addition, other methods utilize highly toxic materials, making such techniques inappropriate for an industrial scale, or require complex processing, or require materials (e.g., sulfuric acid) which need burdensome treatment, and/or have high processing costs. It is desired to provide a high-efficiency industrial process for producing 5-iodo-2-methylbenzoic acid through iodination of 2-methylbenzoic acid as starting material, which is a relatively simple production process and is able to product a high-purity product with high selectivity for the desired product, and provides the desired product at high yield.

Against this background, Applicants have found that iodination of 2-methylbenzoic acid serving as a starting material can be performed at high selectivity through iodinating 2-methylbenzoic acid in the presence of (1) H- $\beta$ -form zeolite, (2) iodine, (3) at least one of iodic acid and periodic acid and (4) both acetic anhydride and acetic acid, and that a high-purity product can be achieved at high yield and high efficiency by combining the reaction step with a purification step including sublimation, distillation and/or crystallization. Note the first full paragraph on page 6 of Applicants'

specification. Note also the paragraph bridging pages 36 and 37 of Applicants' specification.

It is emphasized that the reaction in the presently claimed process is conducted in the presence of (1) H- $\beta$ -form zeolite, (2) iodine, (3) iodic acid and/or periodic acid, and (4) both acetic anhydride and acetic acid. It is respectfully submitted that the results of the present invention are achieved by using all of materials (1)-(4) as in the present claims, as seen in the Examples and Comparative Examples in Applicants' original disclosure.

Thus, compare Example 1 and Comparative Example 4 respectively on pages 18 and 19, and on page 24, of Applicants' specification. It is respectfully submitted that this shows unexpectedly better results in yield and selectivity of 5-iodo-2-methylbenzoic acid, and purity in the crystals, achieved utilizing both acetic anhydride and acetic acid. Similarly, note Example 12 on pages 28 and 29, and Comparative Example 7 on pages 33 and 34, of Applicants' specification, again showing that when both acetic anhydride and acetic acid are used, yield and selectivity of the desired product, and purity in the produced crystal, were unexpectedly improved.

It is respectfully submitted that this evidence in Applicants' specification shows unexpectedly better results achieved by the presently claimed subject matter, overcoming any prima facie case of obviousness even assuming, arguendo, that the teachings of the applied references would have established a prima facie case of obviousness.

Comments by the Examiner in connection with the evidence in Applicants' disclosure, in the paragraph bridging pages 4 and 5 of the Office Action mailed April 4,

2008, are noted. It is respectfully submitted, however, that where Applicants show unexpectedly better results in connection with experimentation with respect to processes even closer than the closest prior art, such evidence must be given great weight in determining the issue of obviousness. See Manual of Patent Examining Procedure (MPEP) 716.02(e), Subsection I. It is respectfully submitted that the evidence in Applicants' specification presents such comparison with processes even closer than the closest prior art, and is respectfully submitted that the experimental data establishes unobviousness of the presently claimed invention.

Attention is also directed to Examples 1, 3, 4, 12 and 14, on pages 18-21 and 28-31 of Applicants specification, as compared with Comparative Examples 5 and 7 on pages 31-34 of Applicants' specification. The Examples 1, 3, 4, 12 and 14 include acetic anhydride, whereas the Comparative Examples 5 and 7 do not. Note, especially, the comparison between Example 12 and Comparative Example 7, the difference therebetween being that in Comparative Example 7 acetic anhydride was not employed. It is respectfully submitted that these Examples and Comparative Examples show that through the present invention, wherein the reaction takes place in the presence of both acetic acid and acetic anhydride, an unexpectedly large conversion of iodine is achieved, whereby iodine content in the crystals is unexpectedly and advantageously decreased according to the present invention avoiding the need for separation and recovery of an unduly large amount of remaining iodine in the purification step. It is respectfully submitted that this evidence of unexpectedly reduced amount of iodine shows further unexpectedly better results achieved according to the present invention,

further supporting a conclusion of unobviousness of the presently claimed subject matter.

Attention is also respectfully directed to Example 1 on pages 18 and 19 of Applicants' specification, together with Examples 2 and 3 on pages 19-21 thereof. Note also Comparative Example 1 on pages 21 and 22 of Applicants' specification, using a reaction mixture including sulfuric acid (compare with the process in Japanese Patent Document No. 2003-012597, wherein 2-methylbenzoic acid was reacted with iodine and periodic acid in the presence of sulfuric acid in AcOH). Note also Comparative Example 2, also including sulfuric acid in the reaction mixture. Note that in Comparative Example 3, the procedure of Example 1 was repeated, except that iodic acid was not employed. As can be appreciated from disclosures on pages 21-24 of Applicants' specification, unsatisfactory results were achieved in each of the Comparative Examples 1-3.

See also the other Examples and Comparative Examples in Applicants' specification; in this regard, note Comparative Example 5 on pages 31 and 32, which shows that when concentrated sulfuric acid was employed as an acid catalyst, purity and yield of 5-iodo-2-methylbenzoic acid were unsatisfactory; and Comparative Example 6 on pages 32 and 33, disclosing that when sulfuric acid was employed as an acid catalyst, the formed 5-iodo-2-methylbenzoic acid crystals had a high iodine content, so that high-purity 5-iodo-2-methylbenzoic acid was not produced.

As can be seen from the foregoing, as well as from a full review of the Examples and Comparative Examples in Applicants' specification, it can be seen that by conducting the iodination reaction in the presence (1) the H- $\beta$ -form zeolite, (2) iodine,



(3) iodic acid and/or periodic acid and (4) both acetic anhydride and acetic acid, unexpectedly better results in selectivity and yield, as well as high purity, are achieved.

It is respectfully submitted that the advantageous results achieved by the present invention would have been unexpected, and it is respectfully submitted that the unexpectedly better results achieved according to the present invention support a conclusion of unobviousness thereof.

Igari, et al. discloses a method for producing monoiodo compounds of methylbenzoate, wherein such compounds are produced by directly iodizing methylbenzoate, a raw material, by using an iodizing agent together with an acid catalyst in a solvent. Specifically, this patent document discloses reacting 2-methylbenzoic acid with iodine and periodic acid in the presence of  $H_2SO_4$  in AcOH. Note the English Abstract of Igari, et al., as well as paragraphs [0001], [0006] and [0010] of the machine generated English translation thereof enclosed with the Office Action mailed April 4, 2008.

Aizawa discloses a method for separating and purifying an isomer mixture of iodo-2-methylbenzoic acid, the method changing the iodo-2-methylbenzoic acid mixture comprising 3-iodo-2-methylbenzoic acid and 5-iodo-2-methylbenzoic acid to corresponding metal salts, adjusting the pH of the aqueous solution of the metal salts to  $5.0 \pm 0.5$  at normal temperatures, and separating precipitating crystals as 5-iodo-2-methylbenzoic acid as a principal compound by filtration, and separating the 3-iodo-2-methylbenzoic acid as a principal compound by adjusting the pH of the filtrate to 3.0-2.0 by addition of an acid. Note the English abstract of Aizawa, et al., as well as

paragraphs [0001], [0007] and [0016] of the machine-generated English translation thereof enclosed with the Office Action mailed April 4, 2008.

It is respectfully submitted that neither of Igari, et al. or Aizawa, et al., either alone or in combination, would have disclosed or would have suggested such a process as in the present claims, including the reaction being conducted in the presence of all of (1) H- $\beta$ -form zeolite, (2) iodine, (3) periodic acid and/or iodic acid and (4) both acetic anhydride and acetic acid, and advantages achieved due thereto.

It is respectfully submitted that the additional teachings of Singh, et al., even in light of the combined teachings of Igari, et al. and Aizawa, et al., would not have rectified the deficiencies of the teachings of Aizawa, et al. and Igari, et al., such that the presently claimed invention as a whole would have been obvious to one of ordinary skill in the art.

Singh, et al. discloses a process for the preparation of halocumenes. The process includes reacting cumene with a halogenating agent in a liquid phase in the presence of an aliphatic carboxylic acid and a specified microporous zeolite catalyst. Note column 2, lines 19-32. See also column 2, lines 49-56.

Initially, it is respectfully submitted that the teachings of Singh, et al. would not have been properly combinable with the teachings of the two applied Japanese patent documents. Thus, each of the two applied Japanese patent documents is directed to providing iodo compounds of methylbenzoic acid or ester thereof. In contrast, Singh, et al. is directed to preparation of 4-halocumenes. In view of different technologies involved in the two Japanese patent documents, on the one hand, and in Singh, et al., on the other, and in view of different problems addressed by each, it is respectfully

submitted that one of ordinary skill in the art concerned with in the two Japanese patent documents would not have looked to the teachings of Singh, et al.

Furthermore, in view of the different technologies, as well as different problems addressed by the applied references, as discussed previously, it is respectfully submitted that there would have been no reason to combine the teachings of the applied references, as combined by the Examiner, absent hindsight use of Applicants' disclosure, which of course is improper under the requirements of 35 USC 103.

In any event, even assuming, arguendo, that the teachings of the three references applied by the Examiner were properly combinable, such combined teachings would have neither disclosed nor would have suggested the presently claimed process, including wherein the reaction takes place in the presence of all of H- $\beta$ -form acetic acid, iodine, periodic acid and/or iodic acid, and both acetic anhydride and acetic acid.

The contentions by the Examiner in the last paragraph on page 5, and the second paragraph on page 6, of the Office Action mailed April 4, 2008, are noted. The Examiner contends that Singh, et al, is reasonably pertinent to the particular problem of the present invention because Singh, et al, teaches iodination of aromatic compounds. This contention by the Examiner in connection with the teachings of Singh, et al, is overly broad and thus is respectfully traversed. It is respectfully submitted that Singh, et al, is directed specifically to preparation of 4-halocumenes by reaction of cumene (i.e., is not directed generally to iodination of aromatic compounds). Moreover, it is respectfully submitted that Singh, et al, is directed to a catalyst process, catalyst processes being known to have unpredictability. In view of the different reactions in

Singh, et al, and in connection with Aizawa, and Igari, et al, one of ordinary skill in the art concerned with in Aizawa, et al, and Igari, et al, would not have looked to the teachings of Singh, et al.

The contention by the Examiner that Singh, et al, is “reasonably pertinent to the particular problem [apparently, addressed by the present invention]” is respectfully traversed. The present invention is directed to a catalyst process for synthesizing 5-iodo-2-methylbenzoic acid, addressing problems of achieving high yield and increased selectivity, and improved product purity, in a process having reduced cost. In contrast, Singh, et al, is directed to preparation of halo-cumenes, particularly for halocumenes in high selectivity by liquid phase chlorination of cumenes with chlorine gas. Again noting unpredictability of use of different catalysts in different chemical reactions, it is respectfully submitted that the Examiner errs in concluding that Singh, et al, is reasonably pertinent to the particular problem addressed by Applicants.

The contention by the Examiner in the last paragraph on page 5 of the Office Action mailed April 4, 2008, that, in response to Applicants’ argument that there would have been no suggestion to combine the teachings of the references, the “claims require a multitude of elements and it is reasonable for one of ordinary skill in the art to consider these elements being used together”, is noted. It is respectfully submitted that the prior art, either by itself or through knowledge of one of ordinary skill in the art, must provide a reason to combine the teachings of the references. It is respectfully submitted that the basis for combining of the references by the Examiner, i.e., that it is reasonable for one of ordinary skill in the art to consider these elements being used together”, without more, does not provide the necessary reason for combining the teachings of the

applied references. It is emphasized that the Examiner must not use hindsight application of the present invention, for combining teachings of the applied references.

The contention by the Examiner on page 3 of the Office Action mailed April 4, 2008, that Igari, et al, teaches the use of acetic acid as the solvent in the iodination reaction, is noted. It is respectfully submitted that the present claims recite use of both acetic acid and acetic anhydride; and, as discussed previously Applicants' original disclosure shows unexpectedly better results in yield and selectivity, and in reduced iodine content in the crystals, utilizing both acetic acid and acetic anhydride. As discussed in the foregoing, it is respectfully submitted that the teachings of the applied references would have neither disclosed nor would have suggested use of both acetic acid and acetic anhydride, and advantages due thereto.

The contention by the Examiner in the sentence bridging pages 4 and 5 of the Office Action mailed April 4, 2008, that Applicants have not shown convincing side-by-side comparisons with the prior art, is noted. It is respectfully submitted, however, that Applicants have provided comparative examples with processes even closer to the present invention than the closest prior art. In view thereof, it is respectfully submitted that Applicants have provided the necessary comparative data for overcoming any prima facie case of obviousness in connection with the presently claimed subject matter.

In view of the foregoing comments and amendments, entry of the present amendments, and reconsideration and allowance of all claims presently pending in the above-identified application are respectfully requested.

Applicants request any shortage of fees due in connection with the filing of this paper be charged to the Deposit Account of Antonelli, Terry, Stout & Kraus, LLP, Deposit Account No. 01-2135 (case 396.45629X00), and please credit any excess fees to such Deposit Account.

Respectfully submitted,

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